Excessive dynamic airway collapse (EDAC)

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Summary

Excessive dynamic airway collapse (EDAC) defines the pathological collapse and narrowing of the airway lumen by >50%, which is entirely due to the laxity of the posterior wall membrane with structurally intact airway cartilage. It is often mentioned, incidentally and interchangeably, with tracheobronchomalacia (TBM), but it is pathophysiologically and morphologically distinct from TBM. The lung diseases most frequently associated with EDAC are the chronic obstructive pulmonary disease (COPD) and asthma. The incidence of EDAC is 22% in patients with chronic obstructive pulmonary disease (COPD) and/or asthma. The decrease in transmural pressure and the weakening of the posterior muscle membrane fosters the collapse of the airways during coughing and/or forced expiration. In most cases the symptoms of EDAC are ascribed to its accompanying pathologies, while the actual pathology is accidentally individuated through a bronchoscopy or CT scan performed for other reasons. Even when the central EDAC is identified as responsible for symptoms, it is better a conservative approach with medical treatment and NIPPV before committing patients to potentially harmful effects resulting from airway stents or open surgical procedures. This review describes the pathophysiology and epidemiology of EDAC, then distinguishes EDAC from TBM and describes its precipitating factors, clinical presentation, also in addition to covering its potential treatments and prognosis.

KEY WORDS: airway collapse; dynamic bronchoscopy; tracheobronchomalacia; ECAC (excessive central airway collapse); EDAC (excessive dynamic airway collapse).

Introduction

Expiratory central airway collapse (ECAC) is a syndrome comprising two different pathophysiologic entities: excessive dynamic airway collapse (EDAC) and tracheobronchomalacia (TBM). EDAC defines the pathological collapse and narrowing of the airway lumen by >50%, which is entirely due to the laxity of the posterior wall membrane with structurally intact airway cartilage. It is a relatively new disease entity; EDAC is often asymptomatic and diagnosed incidentally. It is also often mentioned, incidentally and interchangeably, with tracheobronchomalacia (TBM), but it is pathophysiologically and morphologically distinct from TBM (1-3). Advances in imaging modalities, including bronchoscopy and dynamic radiographic studies, allow increased recognition and differentiation of dynamic and fixed airway abnormalities (4). This review describes the pathophysiology and epidemiology of EDAC, then distinguishes EDAC from TBM and describes its precipitating factors, clinical presentation, also in addition to covering its potential treatments and prognosis.

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Epidemiology

The lack of standardization in the diagnosis of EDAC and its non-distinction from TBM in the past is an obstacle in defining the epidemiology of this disease. The reported prevalence of TBM and EDAC varies with the study population, the diagnostic methodologies employed, and the criteria used to define airway collapse; TBM and EDAC are present in 4-23% of patients undergoing bronchoscopy for various indications (5-9); in a review (2) the incidence of EDAC is 22% in patients with chronic obstructive pulmonary disease (COPD) and/or asthma.

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In order to reduce the number of false positives in the diagnostic process, EDAC should be defined as such only if clinically relevant during maximal breathing. In clinical practice the definition of EDAC as a >50% lumen reduction is obsolete, since about 80% of healthy volunteers over 45 years of

age reach these values of forced expiration (10); it has been observed that usually a 95% reduction is required to induce a symptomatology that requires therapy (11). Recently a classification has been proposed which is based on objective and quantifiable criteria to be applied before and after treatment in order to assess its efficacy (12).
The criteria of this system can be grouped in 2 sets: the descriptive factors including morphology and etiology, and stratification factors that can be scored objectively. The morphology criterion describes the shape of the airway lumen, which is reduced during expiration as assessed by bronchoscopic or radiological studies. Origin (etiology) describes the underlying mechanism responsible for the abnormality: idiopathic or secondary to other disorders. To describe the functional class, this system used the World Health Organization (WHO) functional impairment scale, because of its easy clinical applicability and because it does not address just dyspnea but the overall impact of symptoms on patient's functional status. The extent criterion describes the location and distribution of the abnormal airway segment as assessed by bronchoscopy or radiographic studies. The severity criterion describes the degree of airway collapse (AC) during expiration. This classification allows the monitoring of the progression or improvement of the disease process and the outcome and durability of different treatment strategies. Five domains are addressed: functional class (F), extent (E), morphology (M), origin (O), and severity of AC (S): FEMOS (Table 1). Outcomes are documented as subscripts, for example F_2 E_2 S_4; this information can be tabulated or plotted to provide a visual temporal treatment map, charting patient progress.

Etiopathogenesis

During expiration, the posterior wall of the trachea and of the mainstem bronchi moves inward, reducing the lumen of the airways. Normally the tone of the smooth muscle keeps the airways open, preventing their collapse. In most chronic respiratory pathologies, however, expiration becomes an active process in order to overcome the loss of elasticity of the airways; thus, the pressure of the airways decreases as the air flow advances through the obstructed airways (Bernoulli effect); this generates a transmural pressure gradient that fosters EDAC: the compressed airway region is called flow-limiting segment (FLS).
Besides, recurring coughing, inflammation and the infections that characterize chronic pulmonary diseases, further weaken the tone of the bronchial smooth muscle contributing to EDAC. Therefore, the decrease in transmural pressure and the weakening of the posterior muscle membrane fosters the collapse of the airways during coughing and/or forced expiration. This effect does not change the cartilage structure of the trachea and of the mainstem bronchi.
In the past, the term DAC (dynamic airway collapse) was mainly used to indicate EDAC and TBM, however, although both cause a reduction of the lumen of the main airways, more recent observations suggest that they are two distinct nosologic entities.
TBM is a weakness of the anterior and/or lateral walls of the main airways caused by a softening of the cartilage. This is the main difference from EDAC, because, when the anterior wall is most involved, its collapse causes a decrease in sagittal diameter (crescent-shaped TBM), whereas a weakness of the lateral walls

Table 1 - Stratification factors from FEMOS classification system for ECAC (*Murgu SD, Colt HG. Tracheobronchomalacia and Excessive Dynamic Airway Collapse. Clin Chest Med 2013;34:527-55*).

	Criterion Grade			
Definition	**1**	**2**	**3**	**4**
Functional status Refers to degree of functional impairment as defined by WHO	Asymptomatic	Symptomatic on exertion	Symptomatic with daily activity	Symptomatic at rest
Extent Defines the length of the tracheobronchial wall affected and the location of the abnormal airway segment	No abnormal AC	1 main, lobar or segmental bronchus or 1 tracheal region (upper, mid or lower)	In 2 contiguous or ≥ 2 non contiguous regions.	In ≥ 2 contiguous regions
Severity Describes the degree of the AC during expiration as documented by bronchoscopic or radiologic studies	Expiratory AC of 0%-50%	Expiratory AC of 50%-75%	Expiratory AC of 75%-100%	Expiratory AC of 100%; the airway walls make contact

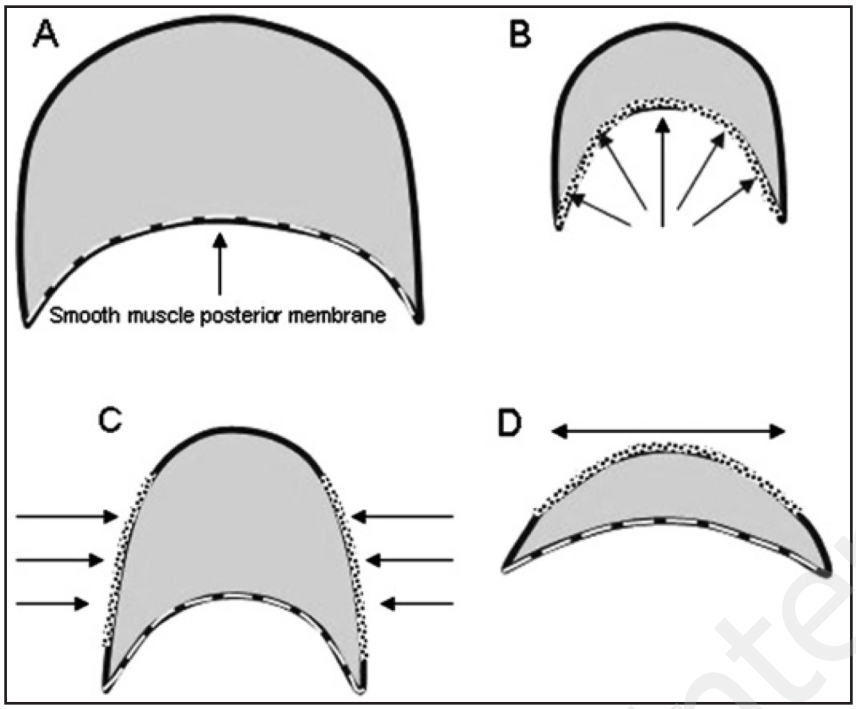

Figure 1 - (A) Normal airway showing smooth muscle posterior membrane. (B) Excessive dynamic airway collapse showing 'bowing' of the posterior membrane and reduction of the cross-sectional airway diameter by <50%. (C) Sabre-sheath tracheobronchomalacia (TBM) affecting the lateral walls of the airway cartilage. (D) Crescent-shaped TBM affecting the anterior walls of the airway cartilage. *Excessive dynamic airway collapse for the internist: new nomenclature or different entity?* (*A Kalra, W Abouzgheib, M Gajera, C Palaniswamy, N Puri, R P Dellinger. Postgrad Med J 2011;87:482-86*).

leads to a decrease in transverse diameter (saber-sheath TBM). Finally, when both the lateral walls and the anterior wall are involved, we observe a concentric diameter reduction (combined TBM), usually combined with great inflammation of the involved structures (polychondritis) (Figure 1). A normal explorative bronchoscopy allows the identification of the weakened cartilage structures. EDAC differs from TBM in that, in this pathology, lumen reduction is entirely due to the laxity and excessive invagination of the posterior wall, by full integrity of the cartilage structures (Figure 2).

The lung diseases most frequently associated with

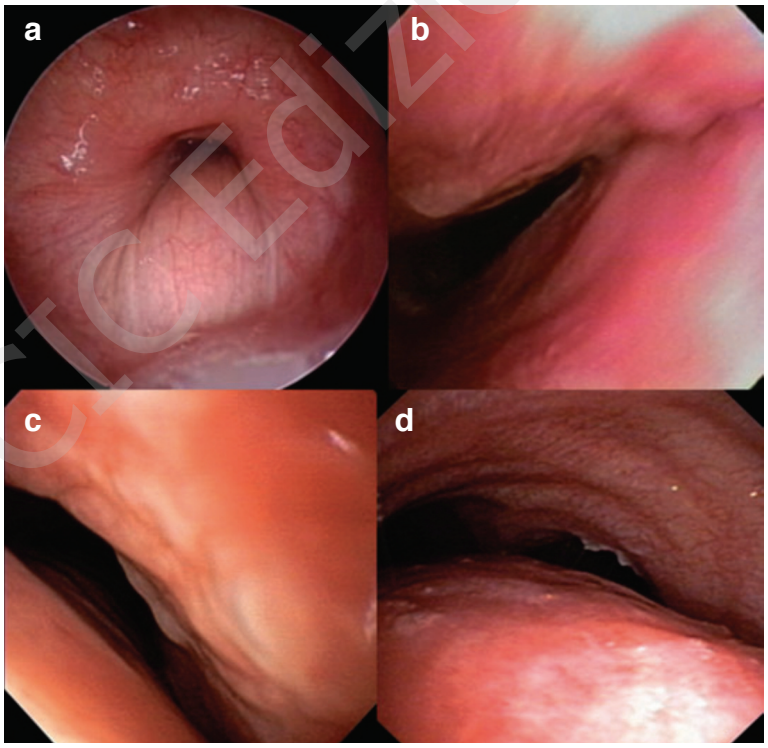

Figure 2 - Morphological types of expiratory central airway collapse. All photos were captured during exhalation. (a) Circumferential- type TBM is characterized by complete collapse of the cartilaginous rings, associated with airway-wall oedema such as in relapsing poly- chondritis. (b) Sabre-sheath-type TBM showing collapse of the lateral airway walls resulting in reduction of the transverse airway diameter. (c) Crescent-type TBM showing collapse of the anterior cartilaginous wall resulting in reduction of the anteroposterior airway diameter. (d) In EDAC, the cartilaginous structures are intact, but there is excessive bulging of the posterior membrane within the airway lumen. EDAC, excessive dynamic airway collapse; TBM, tracheobronchomalacia. (*Murgu SD, Colt HG,. Description of a multidimensional classification system for patients with expiratory central airway collapse. Respirology 2007;12:543-50*).

EDAC are the chronic obstructive pulmonary disease (COPD) and asthma.

Diagnosis

In most cases the symptoms of EDAC are ascribed to its accompanying pathologies (COPD and ASTHMA), while the actual pathology is accidentally individuated through a bronchoscopy or CT scan performed for other reasons. In severe cases the symptomatology is characterized by dry cough, dyspnea, recurrent airways infections due to difficult expectoration and respiratory failure; a typical symptom is a wheezing that resists corticosteroid and bronchodilating therapy. The correct diagnosis is formulated after years or months of investigations and useless treatment of COPD and/or asthma.

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EDAC can be responsible for the problematic weaning of patients from mechanical ventilation, because the endotracheal tube or the positive pressure of the air insufflated into the airways, reduces or prevents the invagination of the posterior tracheal wall; in these cases EDAC diagnosis can be a real challenge for the clinician, as bronchoscopy or TC performed under mechanical (invasive and non-invasive) ventilation could give negative results.

The gold standard for EDAC diagnosis is bronchoscopy; high-resolution dynamic TC represents a good non-invasive diagnostic alternative, whereas pulmonary function testing, while showing the presence of alterations, has no diagnostic value and is not predictive of disease progress.

Bronchoscopy

Bronchoscopy should be preferably performed with a flexible instrument during spontaneous breathing with the patient conscious and alert, so that he/she can follow the instructions of deep breathing, forced expiration and coughing that increase the dynamic collapse of the airways. The patient should change position during the procedure so that the tracheobronchial tree is investigated by performing the above-described maneuvers with the patient laying supine, on the side, or seated. The lumen of the airways is measured in the course of the various maneuvers and the observed anomaly is classified: EDAC, TBM (combined, saber-sheath or crescent-shaped) (13, 14). Attempts have been made to uniform the methods of endoscopic measurement in order to produce an objective quantification of the degree of collapse of the airways, by measuring airway pressure (P_L): the measurement is performed with a double lumen catheter that can measure the P_L simultaneously in two different points of the trachea (15).

When the catheter is positioned with the two holes located on each side of a stenosis, the two pressures plotted against each other show a line with a slope of less than 45° caused by resistance difference between the two points. If the two holes are simultaneously located proximal from or distal to the narrowing, pressures between these sites are in phase, and if plotted against each other, show a straight line with a slope of 45°. By measuring airway pressure proximal and distal to the narrow airway segment and plotting the two pressures against each other during quiet tidal breathing, the site of maximum obstruction and the degree of narrowing can be physiologically assessed, allowing intraoperative prediction of the procedural outcomes. Besides, bronchoscopy allows evaluating the therapeutic efficacy of positive pressure mechanical ventilation (16) or of stenting.

High frequency endobronchial ultrasonography (EBUS) with a radial scanning probe was shown to identify the hypoechoic and hyperechoic layers that correlate with the laminar histologic structures of the central airways. Cartilage abnormalities have been described in patients with malacia caused by tuberculosis, polychondritis. EBUS could potentially distinguish between TBM and EDAC because in the latter it seems that the cartilage is intact, and the posterior membrane is thinner than normal likely because of atrophy of elastic fibers (17).

Computed Tomography (CT)

Low-dose dynamic CT can individuate TBM and EDAC, if static images of end of inspiration and expiration and forced expiration are taken (18).

The maximal collapse may not be detected by paired end-inspiratory CT scans. Therefore, dynamic (kinetic) CT is used in the assessment of TBM and EDAC as an alternative or complementary test to dynamic bronchoscopy, having a similar sensitivity (19). Only specifically trained technicians, who suitably instruct and follow the patient during the procedure, should perform dynamic CT. Three-dimensional renderings are useful to obtain an overall view, but measurements must be taken based on the axial images. Usually three anatomical levels are examined during each phase of the respiratory cycle (aortic arch, main carina, and intermediate bronchus). However, there is no agreement among the studies as to the number and anatomical locations to be analyzed (20).

The advantages of CT over bronchoscopy are, in addition to its lower invasiveness, the possibility to observe the structures surrounding the airways, which can be potentially responsible for the malacia and the characteristics of the lung tissue that contribute to the collapse.

Dynamic CT is often used in pre-operative assessment, to determine the degree, extension and nature of the narrowing (e.g. extrinsic compression) and allows individuating other pathologies requiring different measures.

The advantages of CT over bronchoscopy are, in addition to its lower invasiveness, the possibility to observe the structures surrounding the airways, which can be potentially responsible for the malacia (extrinsic compression) and the characteristics of the lung tissue that

contribute to the collapse (emphysema, bronchiolitis, air trapping). Its disadvantages are the lack of information on the mucosa, the required high patient's compliance and exposure to ionizing radiation.

Pulmonary Function Testing (PFT)

In EDAC patient's spirometry shows an obstructive syndrome, but gives no information as to the severity of the narrowing of the airways (21). Likewise, spirometry does not show the improvements that can follow the application of a stent, tracheoplasty or other therapeutic measures (11). The appearance of the spirometric curve is typical of the dynamic collapse of central airways, but makes no distinction between EDAC and TBM.

AC pattern is characterized by a decrease in flow rate from the peak flow to an inflection point less than 50% of peak flow rate. The inflection point occurs within the first 25% of expired vital capacity. Usually RV and FRC were higher in AC patients, indicating more severe hyperinflation. Flow oscillations on the flow-volume loop have also been described in patients with ECAC. These oscillations take on a saw-tooth appearance, defined as a reproducible sequence of alternating decelerations and accelerations of flow (22).

Treatment

Asymptomatic ECAC, regardless of the degree of AC, should not be treated. Functional impairment in ECAC may result from at least three causes: dyspnea, cough, mucus retention.

Patient's evaluation must include PFT, 6MWT (6 minutes walking test), Karnofsky performance status, dyspnea scale and SGRQ (St George Respiratory Questionnaire).

Once identified on dynamic CT or dynamic bronchoscopy, PFTs are performed to assess if there is any associated impact on maximum expiratory flow or dynamic hyperinflation. A clear categorization as TBM or EDAC is performed and cause is searched for. The extent, degree of narrowing, and impact on functional status and SGRQ are then evaluated to determine if treatment is warranted (23). The cause of process (when known) should be medically treated first, if possible. In addition to disease specific treatment, chest physiotherapy, mucolytic drugs, adjustable positive expiratory pressure valves can be used to improve secretion management (24). If the underlying cause is treated and the patient improves, a follow-up strategy with clinical examination, PFTs, and CT/bronchoscopy is warranted in case of symptom recurrence. If this fails and the patient is critically ill (unable to be weaned from invasive or noninvasive ventilatory support), the airway has to be stabilized and stent insertion is performed (11, 25). If the patient is not critical ill, then NIPPV-assisted bronchoscopy is performed to determine if positive pressure application maintains airway patency. If the airway patency is maintained during NIPPV application, then those particular settings can be prescribed for nighttime NIPVV and intermittent use during the day as triggered by symptoms; application of positive airway pressure serves as a pneumatic stent (26). If the patient does not respond to NIPPV, first strategy involves a so-called stent trial. If there is improvement (objectively documented), tracheoplasty is offered to operable patients (27, 28); if patients are not surgical candidates, a permanent stent insertion is an alternative understanding if there is a high risk for stent related adverse effects: stent migration, obstruction by mucus and granulation tissue, infection, fracture, and airway perforation (26). Alternatively, functional bronchoscopy can be performer to localize the FLS (region of airway compression-Flow Limiting Segment) amenable to stabilization techniques (stent insertion or tracheoplasty). If the FLS are in the trachea or mainstem bronchi, then a stent trial is performed (an algorithm to proceed directly with tracheoplasty has not yet been studied). If the FLS are not in the central airways, then stent insertion or tracheoplasty should not be offered, because they are unlikely to improve flow and alternative explanations for patient's symptoms should be investigated (27, 28). After stent insertion or tracheoplasty, a follow-up bronchoscopy or dynamic CT should be performed within 4 to 6 weeks to assess airway patency and potential adverse events. Even when the central AC is identified as responsible for symptoms, it is better a conservative approach with medical treatment and NIPPV before committing patients to potentially harmful effects resulting from airway stents or open surgical procedures (25).

In addition to disease specific treatment, chest physiotherapy, mucolytic drugs, adjustable positive expiratory pressure valves can be used to improve secretion management.

Even when the central AC is identified as responsible for the symptoms, it is better a conservative approach with medical and NIPPV before committing patients to potentially harmful effects resulting from airway stents or open surgical procedures.

References

1. Murgu SD, Colt HG. Tracheobronchomalacia and excessive dynamic airway collapse. Respirology 2006;11:388-406.
2. Park JG, Edell ES. Dynamic airway collapse. Different from tracheomalacia. Rev Port Pneumol 2005;11:600-2.
3. Murgu SD, Cherrison LJ, Colt HG. Respiratory failure due to expiratory central airway collapse. Respir Care 2007;52:752-4.
4. Murgu SD, Colt HG. Tracheobronchomalacia and excessive dynamic airway collapse: novel diagnostic tools clarify the issues. Pulmon. Perspect. 2005;22:7-10.
5. Kalra A, Abouzgheib W, Gajera M, Palaniswamy C, Puri N, Dellinger R P. Excessive dynamic airway collapse for the internist: new nomenclature or different entity? Postgrad Med J 2011;87:482-486.
6. Jokinen K, Palva T, Sutinen S, Nuutinen J. Acquired tracheobronchomalacia. Ann Clin Res 1977;9:52-7.

7. Jokinen K, Palva T, Nuutinen J. Chronic bronchitis. A bronchologic evaluation. ORL 1976;38:178-86.
8. Ikeda S, Hanawa T, Konishi T. Diagnosis, incidence, clinicopathology and surgical treatment of acquired tracheobronchomalacia. Nihon Kyobu Shikkan Gakkai Zasshi 1992;30:1028-35.
9. Palombini BC, Villanova CA, Araujo. A pathogenic triad in chronic cough: asthma, postnasal drip syndrome, and gastroesophageal reflux disease. Chest 1999;116:279-84.
10. Boiselle PM, O'Donnel CR, Bankier AA. Tracheal collapsibility in healthy volunteers during forced expiration: assessment with multidetector CT. Radiology 2009; 2009:252:255-62.
11. Ernst A, Majid A, Feller-Kopman D. Airway stabilization with silicone stents for treating adult tracheobroncomalacia: a prospective observational study. Chest 2007;132:609-16.
12. Murgu SD, Colt HG. Description of a multidimensional classification system for patients with expiratory central airway collapse. Respirology 2007;12:543-50.
13. Dorfell WV, Fietze I, Hentschel D. A new bronchoscopic method to measure airway size. Eur Respir J 1999;14:783-8.
14. Forkert L, Watanabe H, Sutherland K, Vincent S, Fisher JT. Quantitative videobronchoscopy: a new technique to assess airway caliber. Am J Respir Crit Care Med 1996;154:1794-803.
15. Nishine H, Hiramoto T, Kida H. Assessing the site of maximal obstruction in the trachea using lateral pressure measurement during bronchoscopy. Am J Respir Crit Care Med 2012 185:24-33.
16. Murgu SD, Pecson J, Colt HG. Bronchoscopy on non invasive positive pressure ventilation: indications and technique. Respir Care 2010;55:595-600.
17. Murgu S, Kurimoto N, Colt H. Endobronchial ultrasound morphology of expiratory central airway collapse. Respirology 2008;13:315-9.
18. Lee KS, Sun MR, Ernst A. Comparison of dynamic expiratory CT with bronchoscopy for diagnosing airway malacia: a pilot evaluation. Chest 2007;131:758-64.
19. Baroni RH, Feller-Kopman D, Nishino M. Tracho-broncomalacia: comparison between end-expiratory and dynamic expiratory CT for evaluation of central airway collapse. Radiology 2005;235:635-41.
20. Boiselle PM, Michaud G, Roberts DH. Dynamic expiratory tracheal collapse in COPD: correlation with clinical and physiological parameters. Chest 2012;142:1539-44.
21. Loring SH, O'Donnell CR, Feller-Kopman DJ. Central airway mechanics and flow limitation in acquired tracheobroncomalacia. Chest 2007;131:1118-24.
22. Vincken WG, Cosio MG. Flow oscillations on the flow volume loop: clinical and physiological implications. Eur Respir J 1989;2:543-9.
23. Murgu S, Colt H. Tracheobroncomalacia and Excessive Dynamic Airway Collapse. Clin Chest Med 2013;34:527-555.
24. Jayamanne DS, Epstein H, Goldring RM. Flow-volume curve contour in COPD: correlation with pulmonary mechanics. Chest 1980;77:749-57.
25. Murgu SD, Colt HG. Complications of silicone stent insertion in patients with expiratory central airway collapse. Ann Thorac Surg 2007;84:1870-7.
26. Sirithangkul S, Ranganathan S, Robinson PJ. Positive expiratory pressure to enhance cough effectiveness in tracheomalacia. J Med Assoc Thai 2010;93 (Suppl 6):S112-8.
27. Wright CD, Grillo HC, Hammoud ZT. Tracheoplasty for expiratory collapse of central airways. Ann Thorac Surg 2005;80:259-67.
28. Gangadharan SP, Bakhos CT, Majid A. Technical aspects and outcomes of tracheobronchoplasty for severe tracheobronchomalacia. Ann Thorac Surg 2011;91:1574-80.